



Status Report: Antibiotic Resistance in Maryland Addressing the Urgent Threats

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KEY TERMS

CRE (Carbapenem-resistant *Enterobacteriaceae*) = a family of bacteria that are difficult to treat because they have high levels of resistance to antibiotics, including the carbapenem antibiotics.

MDRO (Multi-Drug Resistant Organisms) = microorganisms, predominantly bacteria, that are resistant to one or more classes of antimicrobial agents (e.g. penicillins, cephalosporins, etc.)

Carbapenems = a group of antibiotics that are usually reserved to treat serious infections, particularly infections caused by bacteria that are highly resistant to antibiotics. Carbapenems are considered antibiotics of last resort for some infections.

Antibiogram = a cumulative antibiotic resistance report. Numbers represent the percent of tested specimens that are susceptible to a particular antibiotic.

Antimicrobial = a type of drug that kills or stops the growth of microbes, including bacteria, viruses, fungi, and parasites.

Antibiotic = a type of drug that kills or stops the growth of bacteria, but not necessarily other kinds of microbes. Examples include penicillin, imipenem, and ciprofloxacin.

Antibiotic Resistance = the ability of bacteria to resist the effects of an antibiotic – that is, the bacteria are not killed, and their growth is not stopped. Resistant bacteria survive exposure to the antibiotic and continue to multiply in the body, potentially causing more harm and spreading to people or other animals.

Antibiotic/Antimicrobial Stewardship Program = a set of coordinated interventions for improving antibiotic use that help ensure that patients get the right antibiotics at the right time for the right duration. A stewardship program protects current patients from getting unnecessary antibiotics (which can have side effects) and protects future patients by ensuring that antibiotics continue to work when needed.

Definitions derived from www.cdc.gov.

INTRODUCTION

Antibiotic resistance is a national, even international, concern. There has been an increasing spotlight on antibiotic resistance in the United States, starting with the 2013 Centers for Disease Control and Prevention (CDC) Threat Report¹ on antibiotic resistance, which identified three "urgent threats" facing the nation: Carbapenem-resistant Enterobacteriaceae (CRE), *Clostridium difficile*, and drug-resistant *Neisseria gonorrhoeae*. This led to the September 2014 *National Strategy for Combating Antibiotic-Resistant Bacteria*², and the March 2015 *National Action Plan for Combating Antibiotic-Resistant Bacteria*³ whose first goal is to slow the emergence and spread of resistant bacteria.

The Maryland Department of Health and Mental Hygiene (DHMH) is engaged in numerous activities that align with the *National Action Plan*, highlighted subsequently in this report. Multidrug-resistant organisms (MDROs) are already widely prevalent across the state. For example, a 2010 prevalence survey of hospital and long-term care patients demonstrated that 34% of mechanically-ventilated patients were infected or colonized with *Acinetobacter baumannii*, and over half of those isolates were multidrug-resistant. DHMH tracks antimicrobial resistance and related infections, including *Clostridium difficile* infection (CDI), through a variety of surveillance programs, including statewide reportable disease surveillance, surveillance conducted as part of the Emerging Infections Program (a partnership between DHMH, the CDC, and 9 other EIP states), the National Healthcare Safety Network, and other collaborative efforts. This report highlights the most urgent antibiotic resistant threats facing Maryland, including CRE, CDI, and drug-resistant *Neisseria gonorrhoeae*.

Carbapenem-resistant Enterobacteriaceae (CRE) Surveillance

Carbapenem-resistant *Enterobacteriaceae* (CRE) are a major and increasing cause of morbidity and mortality throughout the world, including in the United States. CDC estimates that around 9,300 CRE infections occur every year in this country. Up to half of all bloodstream infections caused by CRE result in death. And each year, approximately 600 deaths result from infections caused by the two most common types of CRE, carbapenem-resistant *Klebsiella* species and carbapenem-resistant *E. coli*. In addition to carbapenem resistance, CRE often carry genes that confer high levels of resistance to many other antimicrobials, leaving very limited therapeutic options. Consequently, CRE are considered an urgent public health threat. The National Strategy for Combating Antibiotic-Resistant Bacteria established a national target that by 2020, hospital-acquired CRE infections be reduced by 60% compared to estimates from 2011.

Since November 2013, CRE have been reportable in Maryland, to DHMH. All clinical laboratories in Maryland are required to report cases of CRE meeting the surveillance definition to the DHMH Infectious Disease Epidemiology and Outbreak Response Bureau (IDEORB) within one business day, and submit isolates to the DHMH Laboratories Administration (the state public health lab). In 2015, DHMH revised the definition to align with the definition used nationally for the National Healthcare Safety Network (NHSN) MDRO module. As of January 15, 2015 clinical labs in Maryland are required to report any *Enterobacteriaceae* isolated from any source that is resistant to any carbapenem (doripenem, ertapenem, imipenem or meropenem) OR that is found to be a carbapenemase-producer via Modified Hodge Test, Carba-NP test, MBL-screen or PCR. This new definition is designed to be extremely sensitive for carbapenemase-producing organisms while minimizing the number of false positives.

¹ http://www.cdc.gov/drugresistance/threat-report-2013/

² https://www.whitehouse.gov/sites/default/files/docs/carb national strategy.pdf

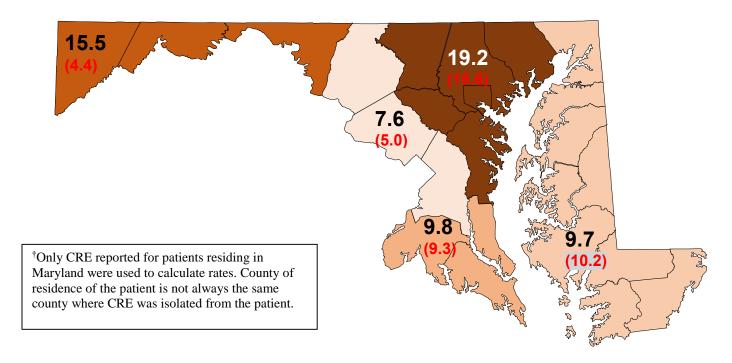
https://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibotic-resistant_bacteria.pdf

Maryland DHMH's IDEORB has received reports of CRE from every jurisdiction in Maryland. 599 unique patients with CRE were reported to DHMH in 2014*, and 517 unique patients have been reported through the first 9 months of 2015.

The following figures and analyses are based on incident cases of CRE. A repeat CRE case in the same patient is considered incident if it is a new organism, or if it occurs more than thirty days after the last reported case and is a clinical (non-surveillance) specimen.

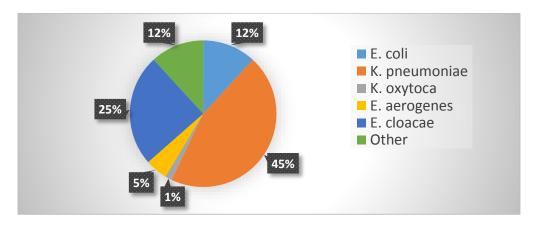
*To ensure comparability, the 2015 CRE definition has been retrospectively applied to 2014 data. Since CRE with any susceptibility to third-generation cephalosporins are excluded from reports in 2014, the adjusted 2014 data may be an under-estimation of 2014 isolates that would have met the 2015 definition.

Maryland CRE rate per 100,000 residents in 2015 (and 2014), by region of patient residence^{\dagger}:



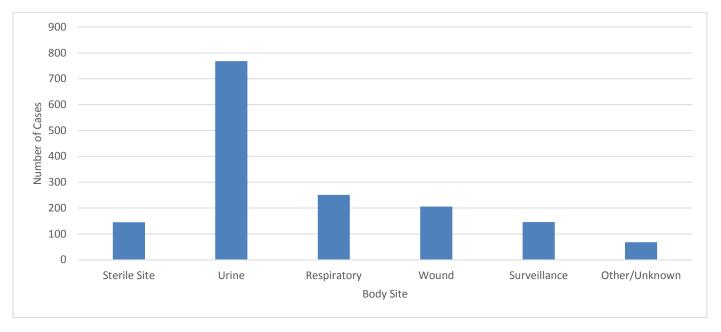
Klebsiella pneumoniae was by far the most frequently reported CRE (48% of reports). *Enterobacter cloacae* made up another 25% of CRE but of these, 76% were resistant to entapenem only.

Maryland CRE by Organism, Jan 2014 – Sep 2015 (Incident cases meeting 2015 definition)



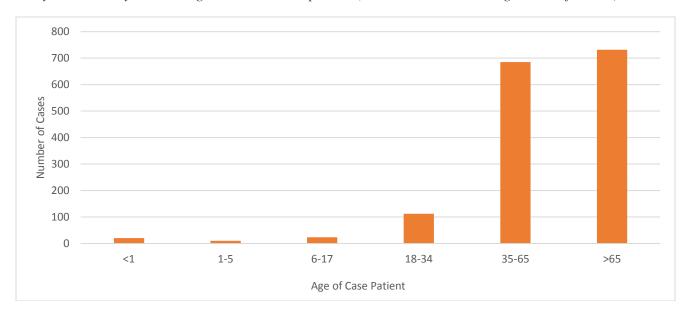
Almost half of all reported CRE were isolated from urine. All other CRE were isolated from normally sterile sites like blood and peritoneal fluid (13%), the respiratory tract (13%), wounds and abscesses (11%), surveillance swabs (11%), and other poorly defined or unknown sites such as "leg", or "body fluid" (5%).





Reported CRE were split evenly by gender with 51% of cases reported in males and 49% in females. CRE occurred more frequently with advancing age. 46% of all reported cases occurred in persons over the age of 65 and another 43% occurred in middle-aged persons aged 35 to 64.

Maryland CRE by Patient Age, Jan 2014 – Sep 2015 (Incident Cases meeting 2015 definition)



The Maryland Laboratories Administration Division of Public Health Microbiology has been performing susceptibility and genetic testing on a subset of isolates collected during 2014 and 2015. Aggregate and facility-specific results will be made available to stakeholders in the near future.

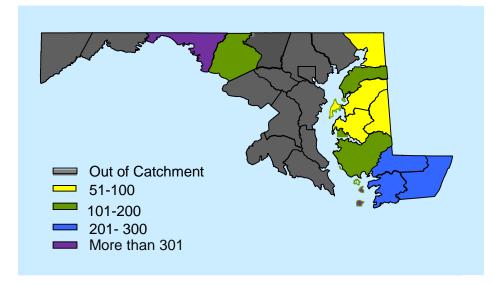
Population Based Clostridium difficile Surveillance

Clostridium difficile can cause severe, even life-threatening, diarrhea and is also considered an urgent public health threat. In 2011, *C. difficile* caused an estimated 500,000 infections in the United States; 29,000 of those resulted in death within 30 days of the initial diagnosis. The National Strategy for Combating Antibiotic-Resistant Bacteria established a target of reducing *C. difficile* infection 50% by 2020 compared to estimates from 2011. Of note, *C. difficile* is not traditionally considered an MDRO. However it is often associated with healthcare exposure and antibiotic use. Since 2011, Maryland has been conducting population based surveillance for *Clostridium difficile* infection (CDI) as part of the Emerging Infections Program. The surveillance catchment area includes Frederick and Washington counties and the Eastern shore with an eligible population of 826,628 people. All laboratories that serve the catchment area, including hospitals, long term care and outpatient facilities submit monthly case line lists to DHMH. All incident cases of CDI get a medical record review to assess for healthcare exposure, medications, underlying conditions and outcomes. Consistently, approximately half of the cases were diagnosed more than 3 days after admission to a cutte or long term care facilities, while half were diagnosed as outpatients or immediately upon admission to a hospital. Standard surveillance is ongoing, along with a survey looking at risk factors in individuals without inpatient healthcare exposure.

CDI Cases by Year, 2011-2014

| Year | Total CDI Cases |
|------|------------------------|
| 2011 | 1,535 |
| 2012 | 1,578 |
| 2013 | 1,377 |
| 2014 | 1,341 |

CDI Incidence Rates by County per 100,000 residents, 2011-2014



Drug-Resistant Gonorrhea

CDC's "Antibiotic Resistance Threats in the United States, 2013" also highlighted *Neisseria gonorrhoeae* as another urgent antibiotic resistance threat. In the United States, *N. gonorrhoeae* bacteria is showing resistance to antibiotics usually used to treat it, including commonly used drugs such as: cefixime (an oral cephalosporin), ceftriaxone (an injectable cephalosporin), azithromycin and tetracycline.

Gonorrhea is the second most commonly reported notifiable infection in Maryland and in the United States. It causes severe reproductive complications and disproportionately affects sexual, racial, and ethnic minorities. Effective gonorrhea control relies on prompt identification and treatment of infected persons and their sex partners. The emergence of cephalosporin resistance, especially ceftriaxone resistance, greatly limits treatment options and can cripple gonorrhea control efforts.

CDC has updated its treatment guidelines to slow the emergence of drug resistance. As of June, 2015, CDC recommends ceftriaxone 250 mg IM PLUS azithromycin 1g PO for treatment of uncomplicated gonorrhea. In 2011, among 321,849 cases of *N. gonorrhoeae* that were reported to CDC, it was estimated that 30% had resistance to at least one antibiotic. Of particular concern is the arrival of cephalosporin resistance seen in other countries. Increasing resistance could result in untreated infections, which potentially leads to increasing complications of gonorrhea, including increased pelvic inflammatory disease, infertility, and susceptibility to HIV infection, in addition to increased healthcare costs and further resistance.

The DHMH laboratories Administration (DHMH Lab), Maryland's state public health laboratory, has the capacity to perform gonorrhea culture and antibiotic sensitivity testing, which are critical to identify emerging resistance in Maryland. While *N. gonorrhoeae* is a reportable disease in Maryland, clinical laboratories are not required to submit specimens for further testing. Thus, the DHMH Lab has access to a limited number of specimens for susceptibility testing. Among specimens tested, the DHMH Lab has yet to identify any ceftriaxone resistance to date, but has identified one cefixime resistant *N. gonorrhoeae* bacterial infection. The resistance rate to ciprofloxacin among isolates submitted to the DHMH Lab is estimated at 25%. Furthermore, an estimated 20-25% of the isolates submitted were resistant to more than one antibiotic (multidrug resistant N. gonorrhea).

Baltimore City data from CDC's 2013 Gonorrhea Isolate Surveillance Project (GISP) suggest that there is some reduced susceptibility to azithromycin among positive cultures from male urethral swabs obtained from Baltimore City Health Department STD Clinic patients. Roughly 20% of isolates submitted had a minimum inhibitory concentration (MIC) of $0.5 \mu g/ml$, and 3% of isolates submitted required a MIC of $1.0 \mu g/ml$.

For additional information on CDC's efforts to identify and prevent resistant gonorrhea infections, see: http://www.cdc.gov/drugresistance/threat-report-2013.

For additional information on sexually transmitted infections in Maryland, see: http://phpa.dhmh.maryland.gov/OIDPCS/CSTIP/Pages/Home.aspx.

Statewide Antibiogram

In 2014, Maryland DHMH required all clinical laboratories to submit an antibiogram for cultures collected in the previous calendar year. A 2013 statewide antibiogram for gram-negative organisms has been compiled and provides a useful overview of antibiotic resistance across the state of Maryland.

Overall, *P. aeruginosa* was the most resistant organism, followed closely by *A. baumannii*. *A. baumannii* was most resistant to carbapenems. *E. coli* was both the most sensitive overall and the most sensitive to carbapenems. This information is summarized in the following tables

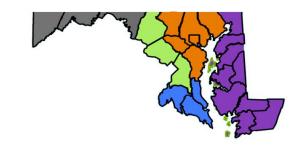
41 of 44 acute care hospitals in the state submitted antibiograms for 2013

- All hospitals reported using Clinical Laboratory Standards Institute (CLSI) guidelines in sample identification and reporting
- Isolates included are from inpatients of all ages and from all specimen sources
- Calculations of total number of isolates susceptible and total number tested may be affected by differences in reporting:
 - o 78% of hospitals reported percent susceptibility as an integer
 - o 73% reported maximum number of isolates tested per organism, so exact sample size per antibiotic is not known

| 2013 Gram Negative Organ Susceptibility | STATEWIDE 41 Hospitals | | | | | | | | | | | |
|--|---------------------------|----------|--------------|--------------|------------|---------|---------------|---------------|--|--|--|--|
| Class | Antibiotic | Organism | A. baumannii | E. aerogenes | E. cloacae | E. coli | K. pneumoniae | P. aeruginosa | | | | |
| | Amikacin | %S | 80 | 99 | 99 | 100 | 97 | 96 | | | | |
| Aminoglycosides | Gentamicin | %S | 64 | 91 | 95 | 89 | 93 | 85 | | | | |
| | Tobramycin | %S | 76 | 90 | 95 | 89 | 90 | 93 | | | | |
| | Amox/Clav | %S | 0 | 1 | 2 | 81 | 83 | 0 | | | | |
| | Ampicillin | %S | 0 | 30 | 1 | 49 | 0 | 0 | | | | |
| Penicillins | Amp/sulb | %S | 74 | 26 | 2 | 56 | 75 | 0 | | | | |
| | Pip/Tazo | %S | 50 | 89 | 77 | 96 | 88 | 92 | | | | |
| | Cefazolin | %S | 0 | 58 | 0 | 86 | 82 | 0 | | | | |
| | Cephalothin | %S | | 0 | 0 | 40 | 79 | | | | | |
| Canhalagnaring | Ceftriaxone | %S | 40 | 85 | 74 | 94 | 87 | 14 | | | | |
| Cephalosporins | Cefotaxime | %S | 33 | 83 | 76 | 94 | 86 | 10 | | | | |
| | Ceftazidime | %S | 57 | 88 | 80 | 93 | 86 | 88 | | | | |
| | Cefepime | %S | 57 | 93 | 93 | 95 | 87 | 86 | | | | |
| | Ertapenem | %S | 0 | 98 | 92 | 100 | 97 | 0 | | | | |
| Carbapenems | Imipenem | %S | 53 | 99 | 98 | 100 | 98 | 87 | | | | |
| | Meropenem | %S | 57 | 98 | 97 | 100 | 97 | 89 | | | | |
| | Ciprofloxacin | %S | 44 | 79 | 90 | 71 | 86 | 74 | | | | |
| Fluoroquinolones | Levofloxacin | %S | 51 | 73 | 92 | 72 | 88 | 74 | | | | |
| | Moxifloxacin | %S | 10 0 | 88 | 92 | 67 | 82 | 39 | | | | |
| | Tetracycline | %S | 47 | 89 | 84 | 71 | 81 | 0 | | | | |
| Tetracyclines | Tigecycline | %S | 92 | 96 | 98 | 100 | 94 | 5 | | | | |
| | Colistin | %S | 95 | 5.0 | 55 | _55 | | 88 | | | | |
| Polypeptides | Polymyxin B | %S | 95 | | | | | 88 | | | | |
| | Aztreonam | %S | 1 | 87 | 75 | 80 | 87 | 73 | | | | |
| Other | Trimeth/Sulfa | %S | 52 | 79 | 87 | 72 | 83 | 0 | | | | |
| | Nitrofurantoin | %S | 0 | 22 | 41 | 96 | 43 | 0 | | | | |

Statewide antibiogram data by geographic region

| Percent Susceptible Gram Negative Organisms by Region | | | | BALTIMORE METRO AREA 24 Hospitals | | | | | NATIONAL CAPITOL REGION 11 Hospitals | | | | | SOUTHERN MARYLAND 3 Hospitals | | | | | | WESTERN MARYLAND 3 Hospitals | | | | | | EASTERN SHORE 5 Hospitals | | | | | | |
|---|----------------|----------|--------------|-----------------------------------|------------|---------|---------------|---------------|--|--------------|------------|---------|---------------|-------------------------------|--------------|--------------|------------|---------|---------------|------------------------------|--------------|--------------|------------|---------|---------------|---------------------------|--------------|--------------|------------|---------|---------------|---------------|
| | Antibiotic | Organism | A. baumannii | E. aerogenes | E. cloacae | E. coli | K. pneumoniae | P. aeruginosa | A. baumannii | E. aerogenes | E. cloacae | E. coli | K. pneumoniae | P. aeruginosa | A. baumannii | E. aerogenes | E. cloacae | E. coli | K. pneumoniae | P. aeruginosa | A. baumannii | E. aerogenes | E. cloacae | E. coli | K. pneumoniae | P. aeruginosa | A. baumannii | E. aerogenes | E. cloacae | E. coli | K. pneumoniae | P. aeruginosa |
| | Amikacin | %S | 81 | 99 | 99 | 100 | 97 | 97 | 71 | 99 | 99 | 99 | 96 | 93 | 100 | 100 | 100 | 99 | 98 | 95 | 70 | 100 | 100 | 100 | 97 | 96 | 93 | 100 | 99 | 99 | 98 | 90 |
| Aminoglycosides | Gentamicin | %S | 65 | 97 | 95 | 88 | 93 | 88 | 47 | 88 | 91 | 89 | 90 | 75 | 83 | 97 | 97 | 91 | 96 | 86 | 60 | 97 | 97 | 91 | 94 | 84 | 91 | 97 | 93 | 89 | 93 | 73 |
| | Tobramycin | %S | 76 | 95 | 95 | 87 | 90 | 94 | 68 | 87 | 92 | 88 | 84 | 86 | 89 | 98 | 98 | 91 | 93 | 95 | 71 | 98 | 96 | 93 | 90 | 94 | 95 | 97 | 93 | 86 | 93 | 89 |
| | Amox/Clav | %S | 0 | 0 | 0 | 78 | 84 | 0 | | 3 | 1 | 82 | 81 | | | | | | | | | | | 84 | 0 | | | 0 | 14 | 77 | 89 | |
| ъ | Ampicillin | %S | 0 | 0 | 0 | 47 | 0 | 0 | 0 | 40 | 3 | 48 | | | | 0 | | 50 | 0 | | | 0 | 0 | 54 | 0 | | 0 | 0 | 52 | 40 | 0 | |
| Penicillins | Amp/sulb | %S | 76 | 0 | 0 | 54 | 74 | 0 | 60 | 45 | 8 | 53 | 70 | | 78 | 0 | 0 | 56 | 77 | | | | | 62 | 73 | | 23 | 0 | 55 | 59 | 83 | |
| | Pip/Tazo | %S | 52 | 76 | 76 | 95 | 87 | 92 | 12 | 95 | 80 | 96 | 87 | 88 | | 89 | 74 | 98 | 88 | 93 | | 83 | 82 | 97 | 92 | 94 | 86 | 80 | 95 | 94 | 92 | 92 |
| | Cefazolin | %S | 0 | 0 | 0 | 84 | 81 | 0 | | 75 | 1 | 84 | 78 | | | 0 | 3 | 89 | 85 | | | 0 | 0 | 92 | 86 | | | 0 | 0 | 82 | 88 | |
| | Cephalothin | %S | | 0 | 0 | 29 | 48 | | | 0 | 0 | 35 | 70 | | | | | | | | | | | | | | 0 | 0 | 37 | 47 | 84 | |
| Cephalosporins | Ceftriaxone | %S | 43 | 71 | 74 | 92 | 87 | 11 | 25 | 90 | 71 | 93 | 82 | 18 | 39 | 88 | 78 | 95 | 89 | | 36 | 82 | 82 | 98 | 89 | | 68 | 80 | 92 | 93 | 72 | 23 |
| Cephaiosporms | Cefotaxime | %S | 35 | 81 | 72 | 94 | 78 | 7 | 24 | 82 | 73 | 93 | 81 | 8 | | | | | | | | | | | | | 70 | 79 | 95 | 95 | 58 | 14 |
| | Ceftazidime | %S | 58 | 74 | 78 | 91 | 82 | 89 | 46 | 90 | 76 | 93 | 81 | 79 | 62 | 84 | 77 | 95 | 88 | 90 | | 95 | 97 | 97 | 93 | 92 | 86 | 84 | 92 | 93 | 92 | 81 |
| | Cefepime | %S | 57 | 96 | 93 | 93 | 87 | 88 | 49 | 92 | 89 | 94 | 82 | 76 | 25 | 100 | 100 | 93 | 91 | 86 | | | | 100 | 0 | 79 | 86 | 94 | 96 | 95 | 89 | 80 |
| | Ertapenem | %S | 0 | 94 | 91 | 100 | 97 | 0 | | 99 | 94 | 99 | 95 | | | 100 | 100 | 100 | 100 | | | 98 | 95 | 100 | 98 | | 100 | 97 | 99 | 99 | 97 | |
| Carbapenems | Imipenem | %S | 57 | 99 | 99 | 100 | 99 | 87 | 27 | 99 | 97 | 100 | 96 | 79 | 61 | 100 | 100 | 100 | 98 | 90 | | 100 | 100 | 100 | 100 | 88 | 100 | 98 | 99 | 99 | 95 | 85 |
| | Meropenem | %S | 56 | 97 | 97 | 100 | 97 | 89 | 45 | 98 | 98 | 100 | 94 | 76 | | | | | | | 81 | 100 | 99 | 100 | 100 | 97 | 95 | 100 | 100 | 100 | 96 | 88 |
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Ciprofloxacin | %S | 43 | 92 | 90 | 68 | 86 | 75 | 32 | 65 | 84 | 70 | 79 | 64 | 62 | 92 | 91 | 75 | 88 | 83 | 65 | 98 | 87 | 76 | 89 | 73 | 84 | 94 | 77 | 69 | 88 | 69 |
| Fluoroquinolones | Levofloxacin | %S | 49 | 94 | 92 | 70 | 88 | 77 | 39 | 65 | 88 | 70 | 81 | 65 | 62 | 94 | 92 | 75 | 89 | 72 | 65 | 98 | 88 | 77 | 91 | 71 | 86 | 94 | 77 | 70 | 89 | 68 |
| 1 luot oquinorones | Moxifloxacin | %S | 10 0 | 96 | 94 | 68 | 87 | 39 | | 81 | 88 | 67 | 78 | | | | | | | | | | | | | | | | 100 | 67 | 80 | |
| Tetracyclines | Tetracycline | %S | 50 | 90 | 85 | 71 | 80 | 0 | 36 | 87 | 78 | 72 | 81 | | | | | | | | | | | | | | 73 | 85 | 75 | 74 | 84 | |
| Tetracyclines | Tigecycline | %S | 92 | 82 | 98 | 100 | 99 | 5 | | 96 | 98 | 100 | 83 | | | | | | | | | | | | | | | 100 | 75 | 100 | 90 | |
| Polypeptides | Colistin | %S | | | | | | | 95 | | | | | 88 | | | | | | | | | | | | | | | | | | |
| 1 orypeputies | Polymyxin B | %S | | | | | | | 95 | | | | | 88 | | | | | | | | | | | | | | | | | | |
| | Aztreonam | %S | 1 | 71 | 74 | 93 | 86 | 75 | | 91 | 76 | 92 | 81 | 62 | | 97 | 65 | 93 | 90 | 74 | 0 | 86 | 87 | 0 | 93 | 75 | 93 | 81 | 93 | 92 | 87 | 61 |
| Other | Trimeth/Sulfa | %S | 53 | 93 | 87 | 70 | 82 | 0 | 37 | 71 | 89 | 72 | 79 | | 68 | 97 | 85 | 76 | 87 | | 60 | 97 | 92 | 78 | 86 | 0 | 86 | 90 | 77 | 73 | 89 | |
| | Nitrofurantoin | %S | 0 | 27 | 47 | 96 | 45 | 0 | | 18 | 21 | 96 | 38 | | | 23 | 17 | 98 | 37 | | | 18 | 30 | 96 | 40 | | 26 | 15 | 94 | 91 | 54 | |
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |



| Percent Suscep Negative Orga Hospital | | | | ST TH | | | (av | | | E THI er of b | | LARGEST THIRD (average number of beds: 397) | | | | | | | | |
|---|-------------------------|----------|--------------|--------------|------------|---------|---------------|---------------|--------------|------------------|------------|--|---------------|---------------|--------------|--------------|------------|----------|---------------|---------------|
| Class | Antibiotic | Organism | A. baumannii | E. aerogenes | E. cloacae | E. coli | K. pneumoniae | P. aeruginosa | A. baumannii | E. aerogenes | E. cloacae | E. coli | K. pneumoniae | P. aeruginosa | A. baumannii | E. aerogenes | E. cloacae | E. coli | K. pneumoniae | P. aeruginosa |
| | Amikacin | %S | 80 | 99 | 100 | 99 | 98 | 95 | 77 | 99 | 99 | 99 | 97 | 96 | 83 | 99 | 99 | 100 | 97 | 96 |
| Aminoglycosides | Gentamicin | %S | 61 | 96 | 96 | 90 | 92 | 82 | 62 | 89 | 94 | 89 | 92 | 85 | 66 | 96 | 95 | 89 | 94 | 85 |
| | Tobramycin | %S | 79 | 97 | 97 | 90 | 90 | 91 | 76 | 88 | 95 | 87 | 89 | 92 | 73 | 94 | 95 | 90 | 90 | 93 |
| | Amox/Clav | %S | | 0 | 8 | 80 | 76 | | 0 | 1 | 0 | 78 | 83 | 0 | | 0 | 0 | 84 | 82 | |
| Penicillins | Ampicillin | %S | | 0 | 0 | 50 | 0 | | 0 | 37 | 2 | 46 | 0 | 0 | 0 | 0 | 0 | 50 | 1 | 0 |
| | Amp/sulb | %S | 70 | 0 | 0 | 56 | 74 | | 73 | 38 | 4 | 52 | 73 | 0 | 76 | 2 | 0 | 59 | 75 | 0 |
| | Pip/Tazo | %S | 34 | 86 | 80 | 96 | 87 | 89 | 50 | 92 | 81 | 95 | 89 | 93 | 61 | 77 | 74 | 96 | 88 | 91 |
| Cephalosporins | Cefazolin | %S | 0 | 0 | 1 | 87 | 78 | | 0 | 72 | 1 | 84 | 83 | 0 | 0 | 0 | 0 | 87 | 82 | 0 |
| | Cephalothin | %S | | 0 | 0 | 34 | 71 | | | 0 | 0 | 36 | 73 | | | 0 | 0 | 43 | 84 | |
| | Ceftriaxone | %S | 39 | 85 | 76 | 94 | 84 | 14 | 29 | 87 | 77 | 93 | 86 | 14 | 52 | 74 | 72 | 94 | 88 | 14 |
| | Cefotaxime | %S | 38 | 88 | 77 | 94 | 82 | 8 | 23 | 79 | 73 | 92 | 85 | 8 | 31 | 80 | 75 | 94 | 85 | 9 |
| | Ceftazidime | %S | 61 | 86 | 80 | 95 | 85 | 85 | 51 | 89 | 83 | 94 | 85 | 88 | 57 | 78 | 76 | 92 | 86 | 86 |
| | Cefepime | %S | 54 | 97 | 91 | 93 | 82 | 7 9 | 53 | 92 | 92 | 93 | 85 | 84 | 60 | 95 | 93 | 96 | 88 | 86 |
| | Ertapenem | %S | | 99 | 95 | 100 | 95 | | 0 | 99 | 96 | 100 | 97 | 0 | 0 | 93 | 90 | 100 | 97 | 0 |
| Carbapenems | Imipenem | %S | 59 | 98 | 99 | 100 | 97 | 83 | 42 | 100 | 98 | 100 | 98 | 86 | 69 | 98 | 98 | 100 | 99 | 87 |
| | Meropenem | %S | 48 | 98 | 98 | 100 | 96 | 80 | 65 | 99 | 99 | 100 | 98 | 90 | 59 | 97 | 97 | 100 | 97 | 87 |
| Florence and the state of | Ciprofloxacin | %S | 39 | 93 | 88 | 72 | 85 | 72 | 44 | 72 | 89 | 69 | 84 | 73 | 47 | 92 | 91 | 72 | 88 | 74 |
| Fluoroquinolones | Levofloxacin | %S | 52 | 94 | 92 | 72 | 86 | 68 | 51 | 70 | 90 | 70 | 88 | 73 | 47 | 92 | 92 | 74 | 88 | 74 |
| | Moxifloxacin | %S | | | 100 | 67 | 80 | | | 75 | 90 | 66 | 79 | 39 | 100 | 97 | 94 | 73 | 91 | _ |
| Tetracyclines | Tetracycline | %S | 41 | 84 | 81 | 73 | 79 | | 47 | 90 | 85 | 70 | 79 | 0 | 49 | 88 | 83 | 71 | 83 | 0 |
| | Tigecycline Colistin | %S | 89 | 90 | 98 | 100 | 96 | | 0.5 | 96 | 97 | 100 | 82 | 0.0 | 95 | | 98 | 100 | 99 | 5 |
| Polypeptides | Polymyxin B | %S | | | | | | | 95 | | | | | 88 | | | | | | |
| | Aztreonam | %S | 0 | 0.2 | 77 | 0.2 | 02 | 67 | 95 | 0.0 | 00 | F0 | O.F. | 88 | 2 | 72 | 72 | 02 | 00 | 72 |
| Other | Trimeth/Sulfa | %S %S | 0 41 | 92 96 | 77 88 | 93 | 83 | 67 | 0 | 89 74 | 80 | 59 72 | 85 | 71 | 2 57 | 73 92 | 72 | 93 71 | 88 | 73 0 |
| Ottler | Nitrofurantoin | %S %S | 41 | | | 73 | 81 | 0 | 52 | 74 | 88 | 72 | 82 | 0 | | | 87 | | 83 | _ |
| | iviliolulalilolli | %5 | | 16 | 32 | 97 | 48 | | 0 | 24 | 21 | 96 | 36 | 0 | 0 | 26 | 53 | 96 | 46 | 0 |

ANTIBIOTIC STEWARDSHIP ACTIVITIES

Outpatient Antibiotic Stewardship Initiative

Maryland is one of 13 states funded for participation in CDC's "Get Smart: Know When Antibiotics Work" campaign. Maryland DHMH's focus has been on technology-based interventions to reduce unnecessary use of antibiotics for upper respiratory infections, such as clinical decision support systems (CDSS). DHMH has collaborated with colleagues at the Baltimore Veterans Affairs Medical Center to evaluate an existing CDSS in their outpatient medical clinics. The CDSS was used to guide provider decision-making and to provide clinical support for safely withholding antibiotics for common upper respiratory infections. Providers were familiarized with the current clinical guidelines for prescribing and were given tools to maintain patient satisfaction during encounters in which antibiotics are not prescribed.

Maryland is also in the process of analyzing statewide outpatient antibiotic prescription data for 2012 and 2013.

Maryland Stewardship Summit



On July 17, 2014 DHMH and the Delmarva Foundation for Medical Care hosted a summit "Implementing Antimicrobial Stewardship in Maryland". The lectures and discussions focused on the science and evidence behind stewardship ("why we must") and practical ways to implement stewardship ("how we can"). Dr. Sara Cosgrove, director of Johns Hopkins Hospital's Antimicrobial Stewardship Program, gave an overview of antimicrobial stewardship and presented on implementation science and its application to stewardship. Dr. Lucy Wilson, Chief of the Center for Surveillance, Infection Prevention, and Outbreak Response within DHMH, discussed stewardship from the state health department's perspective, describing current surveillance data on *Clostridium difficile* and antimicrobial resistance in Maryland, other stewardship-related efforts currently underway in Maryland, and outlining efforts in other states. Our

featured speaker was Dr. Elizabeth Dodds Ashley, the Associate Director for Clinical Pharmacy Services at the University of Rochester Medical Center, who discussed the pivotal role of the hospital pharmacist in implementing an antimicrobial stewardship program, as well as how to implement stewardship programs in facilities with limited resources. We concluded the day with an interactive session on "Getting to How", where participants were assigned to groups based on facility size and type (academic, community, etc.). Each group discussed their ideal antimicrobial stewardship team, interventions they currently have in place and others they would like to implement, and how to measure the effectiveness of their programs. The meeting was a success, attracting 113 participants including infection preventionists, pharmacy directors, and infectious disease physicians representing over two-thirds of Maryland acute care hospitals in addition to other healthcare facilities across the state of Maryland.

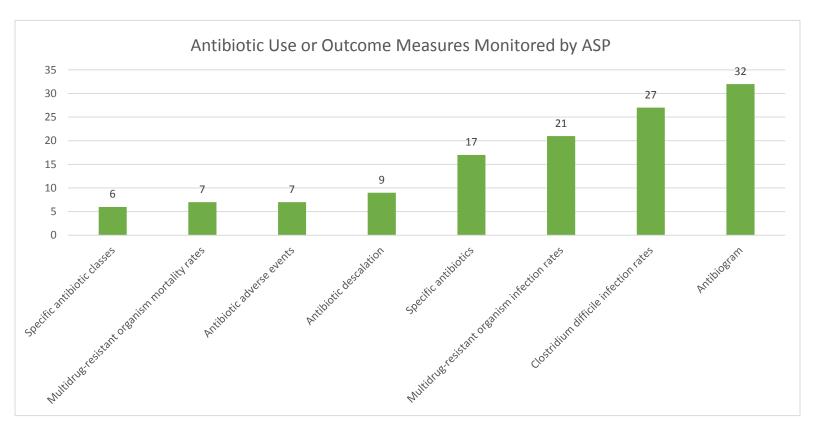
Maryland/Virginia Antibiotic Stewardship Assessment

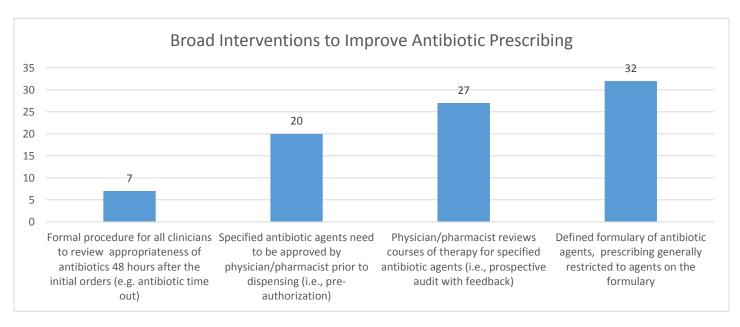
The Virginia/Maryland Antibiotic Stewardship Affinity Group, comprised of representatives from the Maryland Department of Health and Mental Hygiene, the Virginia Department of Health, and the Virginia Health Quality Center, distributed an online assessment to pharmacy and infection prevention contacts within Maryland and Virginia hospitals in October 2015. The baseline assessment characterizes the current state of antibiotic stewardship programs using the seven CDC Core Elements: Leadership Support, Accountability, Drug Expertise, Action,

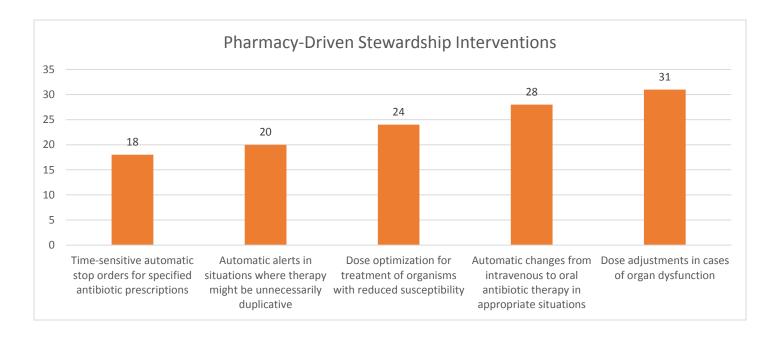
Tracking, Reporting, and Education. A total of 85 hospitals responded, including 33 Maryland hospitals. More than half of respondents (61% in MD) met all seven core elements of hospital ASPs recommended by the CDC.

Among the 33 Maryland hospitals that participated in the survey:

- 18 (55%) have a formal written statement of support from leadership that supports antibiotic stewardship efforts
- 10 (30%) receive either full or partial salary support for one or more antibiotic stewardship team members
- 26 (79%) have a physician leader responsible for program outcomes of stewardship activities
- 32 (97%) have a pharmacist leader responsible for working to improve antibiotic use







Maryland Campaign for Appropriate Antibiotic Use (CAAUSE)

Maryland DHMH, in conjunction with partners from the Maryland HAI Advisory Committee, recently formed a Collaborative to promote antibiotic stewardship across the state, called Maryland Campaign for Appropriate Antibiotic Use (CAAUSE). The goal of this collaborative is to implement and provide support to antibiotic stewardship programs in Maryland acute care hospitals and long term care facilities based on the CDC's 7 Core Elements of Antibiotic Stewardship in hospitals and long term care facilities¹. Members of CAAUSE include facility administrators, pharmacists, infectious disease physicians, and infection preventionists across the healthcare spectrum.

If you would like to be involved in Maryland CAAUSE, please contact Lucy Wilson at lucy.wilson@maryland.gov.

HAI and Antimicrobial Use Prevalence Survey

In May through August of 2011, DHMH, in partnership with the CDC and 9 other Emerging Infections Program states, conducted a Healthcare-Associated Infections and Antimicrobial Use Prevalence Survey. The survey was conducted in 183 hospitals nationally, including 21 Maryland hospitals, and found that approximately 50% of the 11,282 eligible patients were receiving antimicrobial drugs on a single survey day, and 4% of patients had one or more HAIs. Survey results influenced the creation of the "National Strategy for Combating Antibiotic-Resistant Bacteria" and were also used to generate national burden estimates for antibiotic-resistant infections in CDC's report on "Antimicrobial Resistance in the United States, 2013".

This survey is being repeated in 2015 among 22 Maryland hospitals to collect data on how HAI and antimicrobial use prevalence has changed over time as more prevention and stewardship activities are implemented, including an assessment of old vs. new NHSN definitions. Additionally, this year's survey will include an added evaluation of the quality of antimicrobial drug prescribing.

¹ http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html, http://www.cdc.gov/longtermcare/prevention/antibiotic-stewardship.html

WHAT ELSE CAN WE DO?

According to the CDC's Threat Report¹, healthcare facility leaders and providers must join the fight against the spread of CRE and *C. difficile*.

CRE prevention strategies:

- Require and strictly enforce CDC's recommended measures for CRE detection, prevention, tracking, and reporting.
- Make sure your lab can accurately identify CRE and alert clinical and infection prevention staff when these bacteria are present.
- Know CRE trends in your facility and in the facilities around you.
- Know if patients with CRE are hospitalized at your facility, and stay aware of CRE infection risks. Ask if your patients have received medical care somewhere else, including another country.
- Follow infection control recommendations with every patient, using contact precautions for patients with CRE. Whenever possible, dedicate rooms, equipment, and staff to CRE patients.
- Remove temporary medical devices as soon as possible.

C. difficile prevention strategies:

- Support better testing (nucleic acid amplification tests), tracking, and reporting of infections and prevention efforts.
- Ensure policies for rapid detection and isolation of patients with *C. difficile* are in place and followed.
- Assess hospital cleaning to be sure it is performed thoroughly, and augment this using an EPA-approved, spore-killing disinfectant in rooms where *C. difficile* patients are treated.

Common strategies:

- When transferring a patient, require staff to notify the other facility about infections, including CRE and *C. difficile*.
- Prescribe antibiotics wisely. Use culture results to modify prescriptions if needed.
- Participate in regional CRE and/or *C. difficile* prevention efforts.

DHMH supports national recommendations for antimicrobial stewardship in every acute care hospital and long term care facility following CDC's Core Elements of Hospital Antibiotic Stewardship Programs and CDC's Core Elements of Antibiotic Stewardship for Nursing Homes, which includes the following:

- Leadership Commitment: Dedicating necessary human, financial and information technology resources.
- Accountability: Appointing a single leader responsible for program outcomes. Experience with successful programs show that a physician leader is effective.
- Drug Expertise: Appointing a single pharmacist leader responsible for working to improve antibiotic use.
- Action: Implementing recommended actions, such as systemic evaluation of ongoing treatment need after a set period of initial treatment (i.e. "antibiotic time out" after 48 hours).
- Tracking: Monitoring antibiotic prescribing and resistance patterns.
- Reporting: Regular reporting information on antibiotic use and resistance to doctors, nurses and relevant staff.
- Education: Educating healthcare workers, patients, and families about resistance and optimal prescribing.

You can find more information, including a checklist for assessing your facility, here:

Hospitals: http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html

Long Term Care Facilities: http://www.cdc.gov/longtermcare/prevention/antibiotic-stewardship.html

¹ http://www.cdc.gov/drugresistance/threat-report-2013/

RESOURCES

Antimicrobial Stewardship

- CDC's Core Elements of Hospital Antibiotic Stewardship Programs: http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html
 - o Corresponding Checklist: http://www.cdc.gov/getsmart/healthcare/implementation/checklist.html
- CDC's Core Elements of Antibiotic Stewardship for Nursing Homes: http://www.cdc.gov/longtermcare/prevention/antibiotic-stewardship.html
 - Corresponding Checklist: http://www.cdc.gov/longtermcare/pdfs/core-elements-antibioticstewardship-checklist.pdf
- American Hospital Association's Stewardship Toolkit: http://www.ahaphysicianforum.org/resources/appropriate-use/antimicrobial/index.shtml
- Joint Commission Stewardship Toolkit: http://www.jointcommission.org/topics/hai_antimicrobial_stewardship.aspx
- Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Implementing an Antibiotic Stewardship Program: http://cid.oxfordjournals.org/content/early/2016/04/11/cid.ciw118.full.pdf+html
- SHEA's Stewardship Resources: http://www.shea-online.org/PriorityTopics/AntimicrobialStewardship.aspx
- Agency for Healthcare Research and Quality's Toolkit for Reduction of Clostridium difficile Infections
 Through Antimicrobial Stewardship: http://www.ahrq.gov/professionals/quality-patient-safety/patient-safety-resources/cdifftoolkit/index.html
- American Society of Health-System Pharmacists Statement on the Pharmacist's Role in Antimicrobial Stewardship and Infection Prevention and Control: http://www.ashp.org/DocLibrary/BestPractices/SpecificStAntimicrob.aspx
 - Get Smart for Healthcare: http://www.cdc.gov/getsmart/healthcare/
- NHSN's AUR Module: http://www.cdc.gov/nhsn/acute-care-hospital/aur/index.html

CRE

- CDC's Antibiotic Resistance Threats in the United States, 2013: http://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf
- CDC's Facility Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE) November 2015 update to the CRE Toolkit: http://www.cdc.gov/hai/pdfs/cre/CRE-guidance-508.pdf
- DHMH CRE Reporting Requirement: http://dhmh.maryland.gov/laboratories/SitePages/CRE%20Reporting%20Requirement.aspx

Other References

- CDC's Emerging Infections Program: http://www.cdc.gov/ncezid/dpei/eip/
- MHCC Consumer Guide: www.marylandqmdc.org
- National Action Plan for Combating Antibiotic-Resistant Bacteria: https://www.whitehouse.gov/sites/default/files/docs/national_action_plan for combating_antibotic-resistant_bacteria.pdf
- PCAST Report: on *Combating Antibiotic Resistance*: http://www.whitehouse.gov/sites/default/files/microsites/ostp/PCAST/pcast_amr_sept_2014_final.pdf
- White House National Strategy on Combating Antibiotic Resistant Bacteria: http://www.whitehouse.gov/sites/default/files/docs/carb_national_strategy.pdf
- CDC's Antibiotic Resistance Patient Safety Atlas: http://www.cdc.gov/hai/surveillance/ar-patient-safety-atlas.html